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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/625,821	07/22/2003	Satoshi Mori	55022-DIV (71526)	7795
7590 05/07/2008				
Peter F. Corless EDWARDS & ANGELL, LLP P.O. BOX 55874 BOSTON, MA 02205				
EXAMINER				
KUMAR, VINOD				
ART UNIT		PAPER NUMBER		
1638				
MAIL DATE		DELIVERY MODE		
05/07/2008		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/625,821

Applicant(s)

MORI ET AL.

Examiner

VINOD KUMAR

Art Unit

1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 February 2008.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 2, 4, 5 and 8-16 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1, 2, 4, 5 and 8-16 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☒ The drawing(s) filed on 07 February 2008 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. 09/645,825.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

DETAILED ACTION

Status of objections and rejections

1. Amendment filed in the paper of February 7, 2008 is entered.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-2, 4-5 and 8-16 are pending.

Claims 3 and 6-7 are cancelled.

Claims 1-2, 4-5 and 8-16 are examined on merits in this Office action.

The objection to the drawings has been withdrawn in light of amendments to the Figure 10 filed in the paper of February 7, 2008.

The objections to claims 1, 4 and 10 have been withdrawn in light of claim amendments filed in the paper of February 7, 2008.

The rejection of claims 1, 4-5 and 8-16 under 35 U.S.C. 112, 2nd paragraph has been withdrawn in light of claim amendments filed in the paper of February 7, 2008.

The rejection of claims 1, 4-5, 8, 14-15 and 16 under 35 U.S.C. 102(b) as anticipated by Perlak et al. is withdrawn in light of the claim amendments filed in the paper of February 7, 2008.

The rejection of claims 1, 5, 8, 13, 15 and 16 under 35 U.S.C. 102(b) as anticipated by Nayak et al. is withdrawn in light of the claim amendments filed in the paper of February 7, 2008.

Election/Restriction

2. Applicants are reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Objections

3. Claims 5 and 9 remain, and claim 16 is objected to because of following informalities:

Claim 9 remains objected for not reciting SEQ ID NO. for "Kozak sequence".

Applicant traverses the objection in the paper filed on February 7, 2008. Applicant argues that Kozak sequence (ACCATGG) is well known in art, and in view of teachings of the instant specification it is not necessary to refer to this sequence by a sequence identification number.

Applicant's arguments were fully considered but were deemed to be unpersuasive. It is maintained that Kozak sequence must be referred by its sequence identification number to comply with 37 CFR 1.821. Alternatively, Applicant can amend claim 9 by inserting --of ACCATGG-- after "Kozak sequence". There must not be any new matter submitted therefore it is important to note that the specification discloses Kozak sequence as "ACCATGG".

Claim 5 is objected for having improper article before "GT" in line 4. It is suggested to change "a" to --the--. This objection is necessitated due to claim amendment filed in the paper of February 7, 2008.

Claim 16 is objected for not reciting "wherein said seed comprises the heterologous nucleic acid" at the end of the claim. Objection to claim 16 has been necessitated due to the claim amendment filed in the paper of February 7, 2008.

Claim Rejections - 35 USC § 112

4. Claim 2 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons of record stated in the Office action mailed on June 25, 2007.

Claim 2 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite in its recitation "derived", which is confusing, since it is unclear what is retained in the derived product. Applicant traverses the rejection in the paper filed February 7, 2008.

Applicant argues that one ordinary skill in the art will understand the meaning of derived as obtained from (response, pg 8, lines 24-27).

Applicant's arguments were fully considered but were deemed to be unpersuasive. It is maintained that the recitation "derived" is confusing since it is unclear what is retained in the derived product. It is unclear what structure is retained in the derived product. Accordingly, the rejection is maintained.

5. Claims 1-2, 4-5, and 8-16 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for modified yeast FRE1 coding sequence as defined in SEQ ID NO: 1, a transgenic plant and a method of producing said transgenic plant comprising introducing and expressing said coding sequence in said transgenic plant, does not reasonably provide enablement for the scope of possible gene sequences from any species claimed for use in plants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for the reasons of record stated in the Office action mailed on June 25, 2007. Applicant traverses the rejection in the paper filed on February 7, 2008.

Applicant argues that the specification at paragraphs 0024 and 054 sets requirements for methods for transforming a useful plant by introducing another gene into the useful plant using a modified base sequence that can be expressed in the transformed plant with high efficiency. Applicant further argues that examples of transgenic tobacco plants expressing the modified introduced genes are provided in examples 1-9 (response, pg 10, line 25 through line 31 of pg 11). Applicant further argues that the present invention is based on the finding that in the presence of GT-rich base sequence, addition of poly (A) is determined in plants, subsequently mRNA is split at the position at 10-30 bp from the poly (A) signal, for example AATAA like base sequence, then poly (A) is added by an action of poly (A) polymerase. Applicant further argues the present invention is applicable to any heterologous nucleic acid because

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since transcription and addition of poly (A) proceed independently from what is encoded in the heterologous nucleic acid (response, pg 12, lines 12-21).

Applicant's arguments were fully considered but were deemed to be unpersuasive.

Claim 1 is directed to a heterologous nucleic acid sequence from any species that can be modified in a region relating to the poly (A) addition of an mRNA of a plant, and wherein said modification comprises changing the base sequence to a sequence which is not related to the poly (A) addition of the mRNA of said plant. It is maintained that the specification as filed does not provide any other example genes which would require such modification other than the yeast FRE1 gene for expression in tobacco. It is maintained that plant polyadenylation signals do not have a strict consensus requirement. For example, see Grec et al. (Gene 242, 87-95, 2000) who teach cryptic polyadenylation sites within the coding sequences of PDR5 (pleiotropic drug resistance) and MIP (mitochondrial DNA polymerase) genes expressed in tobacco. No AATAAA related elements were found upstream of the cryptic poly A sites of PDR5 or MIP genes expressed in tobacco.

It is further maintained that other than a vague teaching to look for GT-rich areas in any such gene, and change the sequence to remove certain sequences, one of skill in the art would not immediately envision on what is otherwise any possible heterologous nucleic acid gene sequence as broadly claimed.

It is further maintained that the state of art (see e.g. Grec et al.) indicates that the structure of heterologous nucleic acid sequences, i.e. any gene for instance, is

empirically determined and the structural elements of a gene in one species will have different regulatory sequences and different structural elements. Thus there would be an expectation of substantial variation among species encompassed within the scope of the claims because the location of the claimed regions is not readily known absent empirical testing upon use in a plant. It is, therefore, maintained that the specific modifications to the yeast FRE1 gene taught in the specification and claimed as instant SEQ ID NO: 1 do not provide a substantial correlation to any such modification needed or required in any other heterologous nucleic acid sequence broadly claimed.

Additionally, the amended claim 1 recites identifying GT rich sequences having 8 or more consecutive G and/or T nucleotides in the heterologous nucleic acid sequence. The specification does not define GT rich region in the specification. From the claim amendment it appears that the method would require identifying any region in the heterologous nucleic acid sequence having any number of G or T residues. It is therefore, maintained that other than a vague teaching to look for GT-rich (not defined, emphasis added) areas in any such heterologous nucleic acid, and change the sequence to remove certain sequences, one of skill in the art would not immediately envision on what is otherwise any possible heterologous nucleic acid sequence as broadly claimed.

In the absence of adequate guidance, it is maintained that undue experimentation would have been required by a skilled artisan at the time the claimed invention was made to determine how to modify the polyadenylation and GT rich sequence in said heterologous nucleic acid sequence such that the modified

heterologous nucleic acid sequence expresses and produces the functional protein in a transformed plant. See Genentech, Inc. v. Novo Nordisk, A/S, USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

It is, therefore, maintained that given the breadth of the claims, unpredictability of the art and lack of guidance of the specification, as discussed above, undue experimentation would be required by one skilled in the art to make and use the claimed invention commensurate in scope with the claims.

6. Claims 1-2, 4-5, and 8-16 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons of record stated in the Office action mailed on June 25, 2007. Applicant traverses the rejection in the paper filed on February 7, 2008.

Applicant argues that claims have been amended to recite specific polyadenylation signal sequences, and the specification clearly describes factors that are required in a genus of nucleic acid sequences comprising a coding sequence which has been modified to encode a functionally unaltered protein. Applicant further argues that in view of these teachings of the specification and the vast amount of knowledge of codon degeneracy available to one skill in the art, the claimed modified nucleic acid

sequences could be constructed readily such that one of skill in the art would have recognized that applicant was in possession of the sequences as claimed.

Applicant's arguments were fully considered but were deemed to be unpersuasive.

It is maintained that the specification as filed does not provide any other example genes which would require such modification other than the yeast FRE1 gene for expression in tobacco. There would be an expectation of substantial variation among species encompassed within the scope of the claims because the location of the claimed regions is not readily known absent empirical testing upon use in a plant. The specific modifications to the yeast FRE1 gene taught in the specification and claimed as instant SEQ ID NO: 1 do not provide a substantial correlation to any such modification needed or required in any other nucleic acid sequence broadly claimed. One of skill in the art would conclude that Applicant was not in possession of the claimed genus because a description of only one member of this genus is not representative of the variants of the genus and is insufficient to support the claims.

Applicant's attention is drawn to MPEP 608.01(p) which states that Essential material "is defined as that which is necessary to (1) describe the claimed invention..." and such essential material may not be incorporated by reference into the instant specification as filed. It would be essential to know other starting gene sequences which would be applicable to the instantly claimed modifications in order to show that applicant was in possession of a representative number of species of such template sequences at the time the invention was made.

Amended claim 1 requires that the GT rich sequence in the heterologous nucleic acid is 8 or more consecutive G and/or T nucleotides. Amended claim 4 requires that the polyadenylation signal sequence is located downstream from a GT rich base sequence. However, neither the specification nor the prior art described an art recognized definition for what a "8 or more consecutive G and/or T nucleotides" looks like in the region of modification. Likewise, neither the specification nor the prior art described an art recognized definition for what a GT "rich" content looks like in the entire heterologous nucleic acid. It is, therefore, maintained that Applicant has not clearly described the claimed invention such that one of skill in the art would have recognized that Applicant was in possession of a representative number of species of any gene sequence having the optimized consistent use of G+T content since no standard level or placement of G+T content is defined in the specification as filed or the prior art.

It is, therefore, maintained that the specification does not describe these undisclosed structures of Applicant's broadly claimed genus and one skilled in the art cannot reliably predict the structure of these sequences based upon the disclosure of SEQ ID NO: 1. Furthermore, said structures of Applicant's broadly claimed genus are not correlated to the function of preventing cryptic polyadenylation and producing functional protein in a transgenic plant. Further, Applicants have failed to describe conserved functional domains that are shared by these undisclosed structures of their broadly claimed genus.

Accordingly, there is lack of adequate description to inform a skilled artisan that applicant was in possession of the claimed invention at the time of filing. See Written

Description guidelines published in Federal Register/Vol.66, No. 4/Friday, January 5, 2001/Notices; p. 1099-1111.

Given the claim breadth and lack of guidance as discussed above, the specification does not provide written description of the genus broadly claimed. Accordingly, one skilled in the art would not have recognized Applicants to have been in possession of the claimed invention at the time of filing.

Also see in re Curtis (69 USPQ2d 1274 (Fed. Cir.2004)), where the court held that there was sufficient evidence to indicate that one of ordinary skill in the art could not predict the operability of other species other than the single one disclosed in the specification. The court held that a disclosure naming a single species can support a claim to a genus that includes that species if a person of ordinary skill in the art, reading the initial disclosure, would "instantly recall" additional species of the genus already "stored" in the minds, but if other members of the genus would not "naturally occur" to a person of ordinary skill upon reading the disclosure, then unpredictability in performance of species other than specifically enumerated defeats claims to the genus.

For at least these reasons and the reasons of record stated in the previous Office Action, the requirement for written description has not been met. Accordingly, the rejection is maintained.

7. Claims 1-2, 4-5, and 8-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1, line 11, recites "8 or more consecutive G and/or T nucleotides" which introduces **NEW MATTER** into amended claim. The specification does not provide written description support for "8 or more consecutive G and/or T nucleotides".

Dependent claims 2, 4-5 and 8-16 are also rejected because they fail to overcome this deficiency.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1, 4-5, 8, 14, 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Perlak et al. (PNAS, 88:3324-3328, April 1991, Applicant's IDS), and further in view of Joshi (Nucleic Acids Research, 15:9627-9640, 1987). This rejection has been necessitated due to the claim amendment filed in the paper of February 7, 2008.

Perlak et al. teach a method of making a transgenic plant and seeds derived thereof, comprising introducing and expressing a modified coding sequence *cryIA(b)* gene of *Bacillus thuringiensis* in transgenic tobacco and tomato plants. The transgenic plants exhibited improved insect resistance. The modification did not alter the amino

acid sequence of the CryIA(b) protein. The modification of coding sequence for *cryIA(b)* comprised altering AATAAA and/or ATTTA sequences. Furthermore, the modification increased G and C content throughout the region of gene to be introduced, and modification was based on plant preferred codons without changing the amino acid sequence. See in particular, page 3324, abstract; page 3324, 2nd paragraph, materials and methods (modification of the coding sequence of insect control genes) through the end of 2nd paragraph of 1st column of page 3325; page 3325, Table 1; page 3326, Figure 1, Table 2; page 3327, Figure 2, Table 3; Page 3328, 1st column, discussion.

Perlak et al. do not teach GT rich region.

Joshi et al. teach plant gene sequences having GT-rich sequences resembling animal GT-rich sequences found downstream of polyA sites of plant genes. See in particular, page 9627, abstract; page 9628, lines 16-31.

It would have been obvious and within the scope of an ordinary skill in the art to modify the method of modifying heterologous sequence as taught by Perlak et al. by modifying GT rich regions present at 5' end of internal polyadenylation signal sequences. Given that Joshi et al. teach that plant GT rich regions are associated with polydenylation process in plants, one of ordinary skill in the art would have been motivated to modify GT rich regions in said heterologous sequence to prevent premature termination of transcription with a reasonable expectation of success.

9. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Perlak et al. (PNAS, 88:3324-3328, April 1991) in view of Joshi (Nucleic Acids Research, 15:9627-9640, 1987) and Kozak (Nucleic Acids Research, 9:5233-5252, 1981). This

rejection has been necessitated due to the claim amendment filed in the paper of February 7, 2008.

Perlak et al. teachings are discussed supra.

Joshi et al. teachings are discussed supra.

Perlak et al. do not teach Kozak sequence.

Kozak teach that Kozak sequence(s) increases the efficiency of binding of an eukaryotic mRNA to ribosome(s) and thus increasing the efficiency of translation initiation during protein synthesis. See in particular, page 5233, abstract; pages 5234-5236; page 5237, figure 1; table 1; page 5242, table 2, figure 2; page 5347-5249.

It would have been obvious for one of the ordinary skill in the art at the time the claimed invention was made to modify Perlak et al. method for transforming a plant by adding a step of inserting Kozak sequence to the 5' end of translation initiation codon "AUG" in bacterial *cryIA(b)* gene sequence. Given that *cryIA(b)* gene sequence is derived from a bacteria, and Kozak teach that "Kozak sequence" increases the binding efficiency of a mRNA to the eukaryotic ribosome(s), one of ordinary skill in the art would have been motivated at the time the claimed invention was made to insert Kozak sequence(s) in Perlak et al. gene sequence for increasing the efficiency of translation initiation of *cryIA(b)* mRNA transcripts expressed in a plant to produce an insect resistant transgenic plant with a reasonable expectation of success.

Thus, the claimed invention as a whole is prima facie obvious over the combined teachings of the prior art.

Conclusions

10. Claims 1-2, 4-5, and 8-16 remain rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is set to expire within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to VINOD KUMAR whose telephone number is (571)272-4445. The examiner can normally be reached on 8.30 a.m. to 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Phuong T. Bui/

Primary Examiner, Art Unit 1638